

(FILE 'HOME' ENTERED AT 20:58:18 ON 03 JUL 2006)

FILE 'CAPLUS, MEDLINE' ENTERED AT 21:01:44 ON 03 JUL 2006

L1 147 S LIPOSOM? AND OPIOID
L2 46 S L1 AND (FENTANYL OR MORPHINE OR ALFENTANIL OR REMIFENTANIL)
L3 39 DUPLICATE REMOVE L2 (7 DUPLICATES REMOVED)
L4 39 FOCUS L3 1-

L4 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
TI Antinociception and side effects of L- and D-dipalmitoylphosphatidyl
choline liposome-encapsulated alfentanil after spinal
delivery in rats
AB Spinal liposome administration in the rat results in an
allodynia evoked by light touch. It was determined that liposomes
composed of D-isomer phospholipids were essentially non-toxic. The
effects of alfentanil encapsulated in liposomes made
from the natural L-isomer and synthetic D-isomer of dipalmitoyl
phosphatidyl choline on antinociception, side effects, and algogenic
behavior was examined Both unilamellar and multilamellar liposomes
were studied. Rats prepared with chronic intrathecal catheters received
intrathecal injections of alfentanil (5 or 50 µg) in saline
or encapsulated in liposomes composed of either L- or D-isomers
of dipalmitoyl phosphatidyl choline (DPPC) in unilamellar or multilamellar
liposome formulations. Antinociception was measured using the hot
plate test (52.5°). Side effects were measured by catalepsy,
corneal responses, pinna response, righting reflex, and paw step.
Allodynia was measured by lightly stroking the animal's back. Intrathecal
alfentanil in saline or in the liposomes produced a
dose-dependent increased latency in the hot plate response. Encapsulated
of alfentanil in the liposomes produced a significant
decrease in the loss of corneal, paw step and righting reflex and a slight
decrease in catalepsy and loss of the pinna response. There was no
significant difference between liposome preps. in preventing
side effects. L-Multilamellar-DPPC produced allodynia in 100% of the
animals whereas significantly less allodynia was observed with the other
preps. This study indicates that liposomal preps. can
significantly enhance the therapeutic ratio of a lipid soluble opioid
after spinal delivery. However, the choice of lipids for the formulation
of liposomes intended for spinal drug delivery must be
considered since the L-isomer and larger lipid load of multilamellar
liposomes have a direct spinal effect leading to allodynia.
Previous studies have in fact shown that spinal lysolecithin can yield
focal demyelination.

ACCESSION NUMBER: 1995:966750 CAPLUS
DOCUMENT NUMBER: 124:37651
TITLE: Antinociception and side effects of L- and
D-dipalmitoylphosphatidyl choline liposome
-encapsulated alfentanil after spinal
delivery in rats
AUTHOR(S): Isackson, Joel; Wallace, Marks S.; Ho, Rodney J. Y.;
Shen, Danny D.; Yaksh, Tony L.
CORPORATE SOURCE: Dep. Anaesthesiology, Univ. California, San Diego, CA,
USA
SOURCE: Pharmacology & Toxicology (Copenhagen) (1995), 77(5),
333-40
CODEN: PHTOEH; ISSN: 0901-9928
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English

L4 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
TI Antinociception and side effects of liposome-encapsulated
alfentanil after spinal delivery in rats
AB We investigated the spinal antinociceptive and supraspinally mediated side
effects of intrathecal (IT) alfentanil after delivery in saline
or when encapsulated in liposomes of different lipid
constituencies in rats. Rats prepared with chronic IT catheters received IT
injections of alfentanil (1, 3, 10, 30, or 50 µg) prepared in
either saline or in one of three liposome formulations
(dipalmitoyl phosphatidyl choline [DPPC], DPPC containing 20% by weight of
dipalmitoyl phosphatidyl glycerol [DPPC-DPPG], or DPPC containing 20 weight

percent of cholesterol [DPPC-CHOL]). Antinociception was measured by hot-plate (HP) test (52.5°C). In sep. groups of halothane-anesthetized rats, plasma alfentanil concns. were measured (2-120 min) after 50 µg IT alfentanil given in either saline or liposomes. Antinociception was measured by tail withdrawal upon its immersion in water 52.5°C. Supraspinal side effects of the drug were tested by measuring catalepsy and the eye blink evoked by touching the cornea. IT alfentanil in saline produced a dose-dependent increase in the HP response latency and this effect was accompanied by a similar dose-dependent increase in the incidence of catalepsy and blockade of corneal responses, indicating a rapid supraspinal redistribution. The HP dose-response curve for IT alfentanil delivered in liposomes was shifted slightly to the right, as compared to saline vehicle, but liposome encapsulation totally abolished the side effects that were otherwise observed at the highest IT alfentanil dose. The delivery of alfentanil in DPPC-DPPG and DPPC-CHOL liposomes, in comparison to saline, resulted in a significant delay in peak plasma levels, diminished early rostral redistribution of alfentanil, and higher spinal cord levels of alfentanil even at 2 h after administration. Unexpectedly, in control liposomes (without alfentanil), a prominent allodynia (pain behavior evoked by light touch) was observed with all three formulations. The study indicates that liposomal preps. can significantly enhance the therapeutic ratio of a lipid soluble opioid after spinal delivery. The initial findings of allodynia associated with the liposomes, however, suggest the need for systematic studies on the behavioral and tissue toxicol. of these drugs.

ACCESSION NUMBER: 1994:686458 CAPLUS
DOCUMENT NUMBER: 121:286458
TITLE: Antinociception and side effects of liposome
-encapsulated alfentanil after spinal
delivery in rats
AUTHOR(S): Wallace, Mark S.; Yanez, Aladino M.; Ho, Rodney J. Y.;
Shen, Danny D.; Yaksh, Tony L.
CORPORATE SOURCE: Department Anesthesiology, University California San
Diego, La Jolla, CA, 92093-0818, USA
SOURCE: Anesthesia & Analgesia (Baltimore, MD, United States)
(1994), 79(4), 778-86
CODEN: AACRAT; ISSN: 0003-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

L4 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
TI Liposome-encapsulated opioid analgesics
AB Liposome-encapsulated opioid formulations and methods
of use for long-term analgesic activity in animals are provided.
Liposome-encapsulated oxymorphone was prepared and its
pharmacokinetics was studied in rats neuropathic pain model.

ACCESSION NUMBER: 2003:590984 CAPLUS
DOCUMENT NUMBER: 139:138760
TITLE: Liposome-encapsulated opioid
analgesics
INVENTOR(S): Krugner-Higby, Lisa A.; Heath, Timothy D.; Smith,
Lesley J.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003061628	A1	20030731	WO 2003-US1962	20030122
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2473719	AA	20030731	CA 2003-2473719	20030122
US 2003157162	A1	20030821	US 2003-350207	20030122
PRIORITY APPLN. INFO.:			US 2002-350640P	P 20020122
			WO 2003-US1962	W 20030122
REFERENCE COUNT:	2	THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L4 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
TI Sustained tissue drug concentration following inhalation of liposome-encapsulated fentanyl in rabbits
AB Liposomes are microscopic vesicles that can entrap drug mols. Liposomes-encapsulated fentanyl provides sustained drug release following pulmonary administration. In this study, the effect of encapsulation efficiency (EE) of fentanyl within liposomes on the retention of fentanyl within the respiratory tract was examined. Liposomes with 3 different encapsulation efficiencies, 50% EE, 70% EE, were manufactured with radiolabeled fentanyl and phospholipid dipalmitoylphosphatidylcholine. The preps. were administered through an endotracheal tube to anesthetized rabbits, and the respiratory tracts were removed and analyzed for retention of fentanyl and DPPC at different time intervals. Increasing the encapsulation efficiency of fentanyl within liposomes is shown to prolong the retention of both fentanyl within liposomes prolonged the retention of both fentanyl and DPPC with the respiratory tract. The encapsulation efficiency can be manipulated to design a preparation to provide optimal therapeutic plasma fentanyl concns. The unencapsulated or "free" drug could act as a loading dose, and the slow, sustained release of fentanyl from the liposome depot in the lungs could act as a maintenance dose. Thus, this method of delivering a potent opioid, such as fentanyl, has the potential for clin. use in pain management.

ACCESSION NUMBER: 1997:3301 CAPLUS
DOCUMENT NUMBER: 126:108790
TITLE: Sustained tissue drug concentration following inhalation of liposome-encapsulated fentanyl in rabbits
AUTHOR(S): Tan, Stephen; Hung, Orlando; Whynot, Sara; Mezei, Michael
CORPORATE SOURCE: Dep. Anaesthesia Pharmacol., Dalhousie Univ., Halifax, NS, B3H 2Y9, Can.
SOURCE: Drug Delivery (1996), 3(4), 251-254
CODEN: DDELEB; ISSN: 1071-7544
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English

L4 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
TI The effects of intrathecal morphine encapsulated in L- and D-dipalmitoylphosphatidyl choline liposomes on acute nociception in rats
AB Liposomes can serve as a sustained-release carrier system, permitting the spinal delivery of large opioid doses restricting the dose for acute systemic uptake. We evaluated the antinociceptive effects of morphine encapsulated in liposomes of two isomeric phospholipids, L-dipalmitoylphosphatidyl choline (L-DPPC) and D-dipalmitoylphosphatidyl choline (D-DPPC), in comparison with morphine in saline. Sprague-Dawley rats with chronic lumbar intrathecal catheters were tested for their acute nociceptive response using a hindpaw thermal escape test. Their general behavior, motor function, pinna reflex, and corneal reflex were also examined. The duration of antinociception was longer in both liposomal morphine groups than in the free morphine group. The peak antinociceptive effects were observed within 30 min after intrathecal morphine, L-DPPC or D-DPPC morphine injection. The rank order of the area under the effect-time curve for antinociception was L-DPPC morphine > D-DPPC morphine > morphine. The 50% ED was: 2.7 µg (morphine), 4.6 µg (L-DPPC morphine), and 6.4 µg (D-DPPC morphine). D-DPPC morphine had less side effects for a given antinociceptive AUC than morphine. In conclusion, L-DPPC and D-DPPC

liposome encapsulation of morphine prolonged the antinociceptive effect on acute thermal stimulation and could decrease side effects, compared with morphine alone.

ACCESSION NUMBER: 2000:587911 CAPLUS
DOCUMENT NUMBER: 134:36919
TITLE: The effects of intrathecal morphine encapsulated in L- and D-dipalmitoylphosphatidyl choline liposomes on acute nociception in rats
AUTHOR(S): Nishiyama, Tomoki; Ho, Rodney J. Y.; Shen, Danny D.; Yaksh, Tony L.
CORPORATE SOURCE: Department of Anesthesiology, University of California, San Diego, CA, USA
SOURCE: Anesthesia & Analgesia (Baltimore) (2000), 91(2), 423-428
CODEN: AACRAT; ISSN: 0003-2999
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
TI Opioid delivery system for pulmonary administration
AB An opioid formulation for pulmonary administration in the treatment or management of pain, a pulmonary drug delivery device containing, method of administering, kit containing, and uses of same. The formulation contains at least one rapid-onset opioid and preferably also contains a sustained-effect opioid to reduce the frequency of administration. The invention employs the side effects of the opioid formulation to permit patients to self-limit drug intake, thereby avoiding toxicity while achieving analgesia. A pharmacokinetic and pharmacodynamic model is employed to determine optimum drug formulations and optimum parameters for administration. Liposomal fentanyl were prepared and administered to volunteers. The concentration on was 200 µg/mL on the onset, 300 µg/mL during sustained effect and the rate of deposition in the lung was 15-60 µg/min.

ACCESSION NUMBER: 2005:348823 CAPLUS
DOCUMENT NUMBER: 142:379429
TITLE: Opioid delivery system for pulmonary administration
INVENTOR(S): Shafer, Steven Louis; Hung, Orlando Ricardo; Pliura, Diana Helen
PATENT ASSIGNEE(S): Delex Therapeutics Inc., Can.
SOURCE: U.S. Pat. Appl. Publ., 52 pp., Cont.-in-part of U.S. Ser. No. 788,466.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005084523	A1	20050421	US 2004-927145	20040827
US 2004228808	A1	20041118	US 2004-788466	20040301
PRIORITY APPLN. INFO.:			US 2003-450333P	P 20030228
			US 2004-788466	A2 20040301

L4 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
TI Pain management with liposome-encapsulated analgesic drugs
AB Liposome-encapsulated opioid analgesic agents delivered by the pulmonary route provide local, or systemic analgesia superior to that produced by the solution form of these agents administered

by parenteral (i.v., i.m., or s.c. injection) or oral routes. An opioid formulation for inhalation contained fentanyl citrate 40, soy lecithin 5000, cholesterol 500 mg, ethanol 5 mL, and sterile water to 100 mL. The formulation was administered to healthy volunteers through the pulmonary system by inhalation and drug concns. in plasma were monitored to show improved bioavailability.

ACCESSION NUMBER: 1996:126727 CAPLUS
DOCUMENT NUMBER: 124:156099
TITLE: Pain management with liposome-encapsulated analgesic drugs
INVENTOR(S): Mezei, Michael; Hung, Orlando R.
PATENT ASSIGNEE(S): Can.
SOURCE: Can. Pat. Appl., 22 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2119976	AA	19950924	CA 1994-2119976	19940325
CA 2119976	C	19950924		
US 5451408	A	19950919	US 1994-216590	19940323
US 38407	E	20040127	US 2001-880054	20010614
PRIORITY APPLN. INFO.:			US 1994-216590	A 19940323

L4 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2006 ACS on STN
TI Opioid delivery system
AB An opioid formulation for pulmonary administration in the treatment or management of pain and a pulmonary drug delivery device contains at least one rapid-onset opioid and preferably also contains a sustained-effect opioid to reduce the frequency of administration. The invention employs the side effects of the opioid formulation to permit patients to self-limit drug intake, thereby avoiding toxicity while achieving analgesia. A pharmacokinetic and pharmacodynamic model is employed to determine optimum drug formulations and optimum parameters for administration. An example illustrates alfentanil and morphine as examples of opioids in the two drug model.

ACCESSION NUMBER: 2004:740150 CAPLUS
DOCUMENT NUMBER: 141:248744
TITLE: Opioid delivery system
INVENTOR(S): Hung, Orlando Ricardo; Shafer, Steven Louis; Pliura, Diana Helen
PATENT ASSIGNEE(S): Delex Therapeutics Inc., Can.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004075879	A1	20040910	WO 2004-CA303	20040301
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

AU 2004216550	A1	20040910	AU 2004-216550	20040301
EP 1603533	A1	20051214	EP 2004-715861	20040301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004008059	A	20060214	BR 2004-8059	20040301
CN 1780605	A	20060531	CN 2004-80011558	20040301
WO 2005082369	A1	20050909	WO 2004-CA1578	20040827

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2003-450333P	P	20030228
WO 2004-CA303	A	20040301

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 38 OF 39 MEDLINE on STN

TI Liposomes: a new way to deliver pain medications.

ACCESSION NUMBER: 2005359245 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15988187

TITLE: Liposomes: a new way to deliver pain medications.

AUTHOR: D'Arcy Yvonne

CORPORATE SOURCE: Suburban Hospital, Bethesda, MD, USA.

SOURCE: Nursing, (2005 Jul) Vol. 35, No. 7, pp. 17. Ref: 3
Journal code: 7600137. ISSN: 0360-4039.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Nursing Journals

ENTRY MONTH: 200508

ENTRY DATE: Entered STN: 15 Jul 2005
Last Updated on STN: 24 Aug 2005
Entered Medline: 23 Aug 2005